019

THE EFFECT OF LONG-TERM VIGOROUS PHYSICAL ACTIVITY ON KNEE CARTILAGE AMONG ADULTS WITHOUT CLINICAL KNEE DISEASE

A.J. Teichtahl[1], **A.E. Wluka**[1], Y. Wang[1], A. Forbes[1], M.L. Davies-Tuck[1], D.R. English[2,3], G.G. Giles[3], F.M. Cicuttini[1]
[1]Dept. of Epidemiology and Preventive Med., Sch. of Publ. Hlth.and Preventive Med., Monash Univ., Melbourne, Australia; [2]Ctr. for Molecular, Environmental, Genetic and Analytic Epidemiology, Sch. of Population Hlth., Univ. of Melbourne, Melbourne, Australia; [3]Cancer Epidemiology Ctr., The Cancer Council Victoria, Melbourne, Australia

Purpose: Whether participation in long-term vigorous physical activity effects knee cartilage is unclear, and may depend on the state of knee health. In this study, we examined the association between vigorous physical activity levels over a decade, and the subsequent changes in knee cartilage among adults with no clinical knee disease. We then examined whether this effect differed in those with and without bone marrow lesions (BMLs), as an indicator of preclinical joint damage.
Methods: 297 healthy adults aged 50-79 years with no history of knee injury or joint disease were recruited from an existing study. Physical activity and anthropometric data were obtained via questionnaire during 1990-94 and 2003-04 to devise a persistence of vigorous physical activity score. Each subject underwent knee magnetic resonance imaging (MRI) in 2003-04 and again in 2006-07. Cartilage volume, defects and BMLs were measured using validated methods.
Results: Persistent participation in vigorous physical activity over the study period was associated with an increased risk of worsening of medial knee cartilage defects (OR 1.5; 95% CI 1.0 - 2.3). In the subgroup with BMLs, persistent vigorous physical activity was associated with a significant increase in risk of worsening of medial knee cartilage defects (OR 3.4; 95% CI 1.0 - 16.5) and an increased rate of loss of medial knee cartilage volume (21.6 mm^3 per annum, 95% CI -0.4, 43.6). No significant associations were seen in those without BMLs.
Conclusions: In knees with BMLs, persistent participation in vigorous physical activity is associated with adverse cartilage changes in the medial knee compartment. This suggests that the long-term effects of vigorous physical activity on cartilage may depend on the pre-existing health of the joint. In otherwise clinically healthy knees, BMLs identify those likely to have an adverse response to vigorous physical activity.

020

DETERMINANTS OF LONG-TERM RADIOGRAPHIC AND CLINICAL PROGRESSION OF HAND OSTEOARTHRITIS

J. Bijsterbosch, I. Watt, I. Meulenbelt, F.R. Rosendaal, T.W. Huizinga, M. Kloppenburg
Leiden Univ. Med. Ctr., Leiden, Netherlands

Purpose: Little knowledge about the natural history of hand osteoarthritis (HOA) and its determinants is available. Therefore we investigated the determinants of radiographic and clinical progression of HOA over a period of 6 years.
Methods: Radiographic and clinical measures were obtained at baseline and after 6 years in 242 HOA patients (mean age 59.8 yrs, 83% women) participating in the Genetics, ARthrosis and Progression (GARP) study. HOA was defined by the ACR criteria for clinical HOA or the presence of structural abnormalities in the hand (multiple bony swellings/radiological OA). Standardized hand radiographs were scored in pairs in chronological order by consensus opinion of two experienced readers using the OARSI atlas. Osteophytes (OP) and joint space narrowing (JSN) were graded 0-3, and the presence of subchondral erosions (SE) was assessed. Self-reported hand pain and functional limitations were assessed with the Australian/Canadian Osteoarthritis Hand Index LK 3.0 (AUSCAN). A standard diagram of hand joints was used to identify the number of painful joints. During physical examination pain intensity upon lateral pressure in all hand joints was graded 0-3 and the number of bony swellings was recorded. Mean change for AUSCAN, pain intensity, OP and JSN scores were calculated. Radiographic progression was defined as a change in OP or JSN greater than the smallest detectable change (SDC). Logistic regression analysis was used to assess baseline determinants of radiographic progression. Determinants of clinical progression, reflected by change in AUSCAN scores, were evaluated using linear regression. In both analyses adjustments were made for age, sex and body mass index (BMI).
Results: Radiographic progression was present in 53% of patients. The mean (SD) progression in OP and JSN was 1.8 (2.3) and 1.1 (2.0), respectively. The mean (SD) change on AUSCAN pain and function was 0.5 (4.1) and 2.0 (6.8), respectively. The pain intensity score increased with a mean (SD) of 2.7 (7.0). Determinants of radiographic progression, adjusted for age, sex and BMI, are shown in the table. Multiple regression with all determinants showed that the number of bony swellings, OP and the presence of erosive disease remained associated with radiographic progression. The number of painful joints at baseline was positively associated with progression of AUSCAN pain. No other determinants of progression of AUSCAN pain and function were found. Radiographic progression was not associated with change in AUSCAN scores.

Risk of radiographic progression in relation to baseline clinical and radiographic characteristics

	Risk ratio	95% CI
Number of painful joints	1.2	0.9-1.5
AUSCAN pain >7	1.5	1.2-1.7
AUSCAN function >10	1.2	0.9-1.5
Pain intensity score >2	1.4	1.1-1.7
Number of bony swellings > 8	1.8	1.4-2.1
OP score >9	1.8	1.4-1.8
JSN score >18	1.4	1.1-1.6
Number of SE ≥2	1.8	1.5-2.0

Conclusions: Over a period of 6 years considerable radiographic progression of HOA was demonstrated. Structural abnormalities were the strongest determinants of radiographic progression. However, clinical deterioration was less pronounced and difficult to predict from baseline characteristics. Radiographic and clinical progression were not associated. This has implications for the appreciation of clinical outcomes in longitudinal OA studies.

021

PAIN IMPROVEMENTS FOLLOWING TOTAL JOINT REPLACEMENT: WHAT YOU MEASURE MATTERS

A.M. Davis[1], L.S. Lohmander[2], R. Wong[1], V. Venkataramanan[1], G.A. Hawker[3]
[1]Toronto Western Res. Inst., Toronto, ON, Canada; [2]Univ. Hosp. in Lund, Lund, Sweden; [3]Women's Coll. Hosp., Toronto, ON, Canada

Purpose: The Intermittent and Constant Osteoarthritis Pain (ICOAP) measure, a new measure, was developed under an OARSI/OMERACT initiative as one element for determining outcome in DMOAD trials for osteoarthritis (OA) of the hip or knee. It was developed from interviews with people with OA of the hip and knee. It includes 5 items assessing 'constant' hip or knee pain and 6 items assessing 'intermittent' hip or knee pain; item response options are on a 4-point scale from 'not at all' to 'ex-

tremely'. Subscale and total scores are standardized to 0 to 100, where higher scores indicate worse pain. The ICOAP constructs of 'intermittent' and 'constant' pain are conceptually different from other pain measures such as 'pain on activity' as measured by the WOMAC and pain 'intensity' as measured by the Chronic Pain Grade (CPG) often used in people with OA. As primary total hip (THR) and total knee (TKR) replacement are known to be effective in relieving pain, the purpose of this study was to evaluate the responsiveness of the ICOAP and secondarily to evaluate if various pain constructs have similar changes following joint replacement.
Methods: Patients undergoing primary THR or TKR were recruited from a tertiary care centre. They completed the ICOAP, WOMAC pain, HOOS/KOOS pain and the CPG pre surgery and at 6 months post surgery. All measures were scored 0-100 with higher scores representing more pain. Descriptive statistics were calculated for the sample and measures. The standardized response mean (SRM) was calculated for each of the pain measures.
Results: The THR group (n=34) ranged in age from 37-85 years (mean=58.2) with 74% male. The TKR group (n=44) ranged in age from 45-86 years (mean=64.2) with 75% female. Both the THR and TKR groups had significant improvement ($p<.0001$) on all pain measures but the TKR group had smaller improvements on all measures. However, as shown in Tables 1 and 2 the magnitude of change varied by construct, with pain on activity (HOOS, KOOS and WOMAC) improving the most. Additionally, THR patients reported more intermittent pain pre surgery and experienced greater relief post surgery than TKR patients.

Table 1. Hip

	Baseline Mean (std)	Six months Mean (std)	Change Mean (std)	SRM
Constant pain	43.09 (24.80)	09.71 (18.17)	33.38 (22.21)	1.50
Intermittent pain	61.38 (16.31)	16.21 (19.86)	45.18 (19.56)	2.31
Total pain	53.09 (17.83)	13.32 (18.32)	39.76 (17.36)	2.29
WOMAC-Pain	52.79 (14.10)	11.47 (12.94)	41.32 (15.87)	2.60
HOOS-Pain	60.97 (13.35)	14.58 (13.98)	46.38 (15.51)	2.99
Chronic Pain Grade	60.84 (22.31)	12.21 (14.88)	48.26 (23.44)	2.06

Table 2. Knee

	Baseline Mean (std)	Six months Mean (std)	Change Mean (std)	SRM
Constant pain	42.27 (28.78)	15.45 (21.75)	26.82 (32.14)	0.83
Intermittent pain	52.25 (21.08)	23.66 (25.37)	28.59 (27.91)	1.02
Total pain	47.66 (23.12)	19.91 (20.93)	27.75 (27.22)	1.02
WOMAC-Pain	50.80 (20.96)	22.84 (20.78)	27.95 (23.24)	1.20
KOOS-Pain	58.25 (18.95)	28.09 (20.11)	30.16 (20.98)	1.44
Chronic Pain Grade	56.60 (26.10)	22.51 (23.58)	34.79 (30.84)	1.13

Conclusions: This preliminary works demonstrates that the multifaceted constructs of pain are effectively relieved through joint replacement. However, it also confirms the complexity of defining pain and the need to clearly understand the construct of pain being evaluated and how it is impacted by different types of interventions. The HOOS/KOOS pain measures which include the WOMAC pain likely have slightly larger SRMs than the WOMAC as they have more items. Finally, intermittent pain seems to be different in hip versus knee OA.

022

FOLLOW-UP ANALYSIS OF THE ROLE OF GENETIC VARIATION IN ADAMTS14 IN OSTEOARTHRITIS SUSCEPTIBILITY

A. Gonzalez[1], C. Rodriguez-Fontela[1], M. Calaza[1], A. Carr[2], M. Doherty[3], J.J. Gomez-Reino[1,4], J. Loughlin[5], T. Spector[6], A. Tsezou[7], A.M. Valdes[6]
[1]Hosp. Clinico Univ.rio de Santiago, Santiago de Compostela, Spain; [2]Nuffield Orthopaedic Ctr., Oxford, United Kingdom; [3]Univ. of Nothingham, Nottingham, United Kingdom; [4]Univ. of Santiago de Compostela, Santiago de Compostela, Spain; [5]Newcastle Univ., Newcastle upon Tyne, United Kingdom; [6]St. Thomas Hosp. Campus, Kings Coll., London Sch. of Med., London, United Kingdom; [7]Univ. of Thessaly, Larissa, Greece

Purpose: Two of our independent lines of research have shown association of SNPs in ADAMTS14 (the gene for an extracellular matrix protease likely involved in processing of procollagen fibers) with osteoarthritis (OA), predominantly with severe knee OA in women. One of these lines found association with a nsSNP of likely deleterious effect in exon 21 (rs4747096), the other with an unlinked SNP in intron 4 (rs10823602). We aimed to explore possible association of other SNPs in the gene and to confirm these two association signals in new sample collections.
Methods: A total of 28 SNPs were selected in the ADAMTS14 sequence either because they were tagSNPs in the LD blocks containing rs4747096 or rs10823602; or because they were nsSNPs or SNPs affecting probable transcription factor binding sites. These 28 SNPs were genotyped as a screening step in the women from the Oxford collection, which showed the strongest association with rs4747096 in previous studies. Associated SNPs in this screening step were studied in samples from the Santiago, Thessaly and Nottingham collections. Data from the Chingford and TwinsUK collections were also included in some analyses.
Results: The screening step identified 9 SNPs associated with severe knee OA (TKR samples) in women: seven in the rs4747096 LD block and two in the rs10823602 LD block, with one of them the rs10823602 SNP itself. Further analyses by conditional logistic regression and by replication in TKR samples from Santiago and Thessaly reduced the 9 associated SNPs to a single independent association signal corresponding to the rs4747096 nsSNP, which looked as the most likely causal variant. Finally, this nsSNP was studied in the TKR and THR samples from the Nottingham collection. Allele frequencies in these samples showed an opposite trend to the observed in the other collections studied previously. Consequently, global analysis of more than 2900 samples in the TKR side or of more than 3000 in the THR side did not show association. In addition, the rs10823602 SNP was no longer associated in the Chingford, TwinUK and Nottingham collections, where it was first described, once a larger number of samples were analyzed.
Conclusions: Knee OA association with two ADAMTS14 SNPs was obtained in previous studies with some limitations because the rs4747096 association was absent in men and in mild OA cases. Our follow-up analysis indicates that these associations were most likely spurious because they are not consistently replicated in additional sample collections, even in those having the same clinical characteristics showing predominant association in our previous reports.